DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

January 27, 2015

Siemens Healthcare Diagnostics, Inc.
c/o Ms. Fatima Pacheco
Regulatory Clinical Affairs Specialist
511 Benedict Avenue
Tarrytown, NY 10591

Re: k143680

Trade/Device Name: ADVIA Centaur® IgE Master Curve Material
Regulation Number: 21 CFR 862.1660
Regulation Name: Quality control material (assayed and unassayed)
Regulatory Class: Class I, Reserved
Product Code: JJX
Dated: December 19, 2014
Received: January 5, 2015

Dear Ms. Pacheco:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set

forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Leonthena R. Carrington -A

Leonthena Carrington, MS, MBA, MT (ASCP)
Director (Acting)
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k143680

Device Name
ADVIA Centaur® IgE Master Curve Material

Indications for Use *(Describe)*
The ADVIA Centaur® IgE Master Curve Material is for in vitro diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur Total IgE assay.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

SIEMENS

510(k) Summary

510(k) Summary – ADVIA Centaur IgE Master Curve Material

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: k143680

1. Applicant Information

Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591 USA
Contact Person:	Fatima Pacheco Regulatory Clinical Affairs Specialist
Phone Number:	(914) 524-2450
Fax Number:	(914) 524-3579
E-mail Address:	fatima.pacheco@siemens.com
Date Prepared:	January 26, 2015

2. Device Name

Proprietary Name:	**ADVIA Centaur® IgE Master Curve Material**
Measurand:	Quality Control materials for ADVIA Centaur IgE assay
Type of Test:	Master Curve Material (MCM) for ADVIA Centaur IgE assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Immunology (82)

3. Predicate Device Name IMMULITE 2000 Total IgE Calibration Verification Material (CVM)

Predicate 510(k) No: k133122

4. Device Description: ADVIA Centaur® IgE Master Curve Material is an *in vitro* diagnostic product containing various levels of IgE spiked in lyophilized human plasma with sodium azide (0.1%) and preservatives. Each set contains seven levels (MCM1–7); with a reconstituted volume of 1.0 mL/vial per level. MCM1contains no analyte. The MCMs assigned values are lot-specific of target

	values: 0.0, 12.5, 40.0, 270, 1000, 1700, and 3150 IU/mL.
5. <u>Intended Use</u>: **Indication for Use:**	See Indications for Use Statement below: The ADVIA Centaur® IgE Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur Total IgE assay.
Special Conditions for Use Statement(s):	For prescription use only
Special Instrument Requirements:	ADVIA Centaur® Systems A description of the ADVIA Centaur system is documented in k971418. Subsequent modifications to the instrument have been reviewed and cleared in k032525 and k041133.
6. <u>Technological Characteristics and Substantial Equivalence Comparison with Predicate</u>:	A comparison of the device features, intended use, and other information demonstrates that the ADVIA Centaur IgE MCM is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: *Substantial Equivalence Comparison*

SIMILARITIES		
	Candidate Device	**Predicate Device**
Item	ADVIA Centaur IgE MCM	IMMULITE 2000 Total IgE Calibration Verification Material (CVM)
Intended Use	The ADVIA Centaur IgE Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur tIgE assay.	The IMMULITE 2000 Total IgE Calibration Verification Material (CVM) is intended for *in vitro* diagnostic use, as a control for calibration verification of the IMMULITE 2000 Total IgE assay on IMMULITE 2000 systems as indicated in the CVM Package Insert.
Analyte	IgE	Same
DIFFERENCES		
Form	Lyophilized	Liquid
Storage	2–8°C	≤ -20°C
Use	Multiple Use	Single Use
Matrix	Human plasma	Equine serum
Levels	7	4
Stability	**Unopened** – Stable when stored unopened at 2–8°C for 8 months. **Opened (Reconstituted)** – Stable when stored at 2–8°C for 28 days; or on-board for 4 hours.	**Unopened** – Stable until the expiration date on the vial.

7. Standard/Guidance Document References

The following recognized standard and guidance documents were used:

- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

8. Test Principle

The MCMs are specifically intended for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur assays for use on the ADVIA Centaur systems. Customers may use MCMs for bi-annual calibration verification checks of the assay range and linearity in order to meet the requirements of hospital accreditation bodies.

9. Performance Characteristics

9.1 Analytical performance:

The following studies are not applicable for the purpose of this submission:

- *Precision/Reproducibility*
- *Linearity/Assay Reportable Range*
- *Detection limit*
- *Analytical Specificity*
- *Assay cut-off*
- *Method Comparison Studies*
- *Clinical Studies (Sensitivity, Specificity, and cut-off)*

9.2 Non-Clinical Performance Testing

9.2.1 *Stability Studies*

Stability studies were conducted on the ADVIA Centaur system to support the shelf life (unopened) and reconstituted material for the ADVIA Centaur IgE MCMs to ensure that it maintains optimal product performance throughout the established shelf-life. The data supports the stability claims detailed in the ADVIA Centaur IgE MCM Instructions for Use.

The following stability studies were performed for ADVIA Centaur IgE MCM:

- Real Time/Shelf Life (unopened) Stability
- In Use Open Vial (reconstituted) stored at 2–8°C Stability
- On-Board Stability

Real time shelf-life studies (unopened): Test IgE MCMs were stored unopened at 2–8°C and tested at T=0 and at the following time points: 7 months, 8 months, 9 months, 11 months,12 months, 18 months, 35 months and 36 months. Shelf life claims are based upon real time stability carried out one month after the duration claimed. Real time shelf-life stability studies of MCMs were determined by comparison of dose recoveries at T=0. Current testing meets the sponsor's acceptance criteria for the real-time stability study up to the 9 months' time point, which supports a shelf-life claim of 8 months. Storage shelf-life (unopened) at 2–8°C is indicated by the expiration date on the vial label.

In-Use Open Vial (Reconstituted): Test IgE MCMs were reconstituted, each level pooled, aliquotted and stored at 2–8°C, tested in 5 replicates per level at T=0, 7, 14, 21, 28, and 29 days on the ADVIA Centaur XP system. Acceptance criteria for the open vial (reconstituted) stability study were met to the 29 days' time point, which supports the open vial claim of 28 days when properly stored at 2–8°C.

On-board Stability: Pooled aliquots of test IgE MCMs in sample cups were stored on the ADVIA Centaur XP system and measured at time point T=0, 2, 4 and 5 hours. On-board stability studies of MCMs were determined by comparison of dose recoveries to the T=0 dose recovery results. Acceptance criteria for the on-board stability study were met up to 5 hours, which supports the on-board stability claim for 4 hours.

Stability Acceptance Criteria

The stability specifications acceptance criteria for the ADVIA Centaur IgE MCM are as follows:

- Real Time/Shelf life (Unopened): The dose recovery for MCM1 must be ≤ 2.0 IU/mL dose; MCM2–7, the % dose recovery met the sponsor's required acceptance criteria.
- In-Use Open Vial (Reconstituted): The dose recovery for MCM1 must be ≤ 2.0 IU/mL dose; MCM2–7, the % dose recovery met the sponsor's required acceptance criteria.
- On-Board: The dose recovery for MCM1 must be ≤ 2.0 IU/mL dose; MCM2–7, the % dose recovery met the sponsor's required acceptance criteria.

9.2.2 *Value Assignment*

The ADVIA Centaur IgE MCMs are value assigned using assigned reference calibrators and MCMs. The assigned reference calibrators are prepared using IgE stock and are traceable to internal material which is standardized against World Health Organization (WHO) 75/502 reference material. The MCMs are manufactured using qualified materials and measurement procedures.

For each new IgE MCM lot manufactured, MCM1 is run in 5 replicates on two separate runs using one reagent kit lot on the ADVIA Centaur system. A nested testing run protocol is used for MCM2–MCM7 value assignment. This consists of running alternating samples of the reference and new MCM level in the same run. MCM2–MCM7 were tested on 20 replicates in total, comprised of one run and four sample cups run in 5 replicates on one system and one reagent kit lot. This protocol is designed to remove system and run variation. The new MCM doses must fall within the final value assignment specification for IgE MCMs. The MCMs dose values are generated using the two-point calibration. The new MCM dose is calculated based on the relationship between the observed reference MCM dose and its assigned value. A performance verification run consisting of 6 replicates of each MCM level is run using one instrument, one reagent kit lot and Bio-Rad controls. The mean MCM doses of the new MCM lot manufactured must fall within the customer range specifications.

The target for MCM1 is assigned a 0.0 dose. MCM1 is analyte-free basepool comprising of only the matrix and preservatives. The quality control specifications and final value assignment limits for IgE MCM ensure that MCM1 measures at or below the IgE assay sensitivity limit. MCM7 targeted greater than

the assay range is diluted with the MCM1 to meet the reportable range of the assay.

9.2.3 *Expected Values*

The expected values are the lot-specific assigned values obtained at value assignment and the lot-specific assigned ranges are the lot-specific customer ranges are established per the sponsor's internal procedural specifications for IgE MCM.

ADVIA Centaur IgE MCM levels and target values are provided in **Table 2.**

Table 2: *IgE MCM Levels and Target Values*

MCM level	Target Values (IU/mL)
MCM1	0.00
MCM2	12.5
MCM3	40.0
MCM4	270
MCM5	1000
MCM6	1700
MCM7	3150
Assay Range	1.5–3000 IU/mL

9.2.4 *Traceability*

The ADVIA Centaur tIgE assay is standardized against the World Health Organization (WHO) 75/502. Assigned values for calibrators and MCMs are traceable to this standardization. Assigned values for calibrators and MCMs are traceable to this standardization. The IgE MCMs are manufactured using qualified materials and measurement procedures.

10. Proposed Labeling

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

11. Conclusion

The ADVIA Centaur IgE Master Curve Material (MCM) is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed IMMULITE 2000 Total IgE CVM. Based on the testing completed and the comparisons with predicate device, the ADVIA Centaur IgE Master Curve Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.